NTP
National Toxicology Program

Research Concept: *o*-Phthalaldehyde

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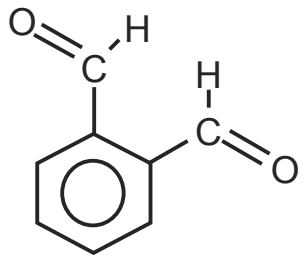
NIEHS/NTP

Nomination: *o*-Phthalaldehyde (OPA)

- Nominated by the National Institute for Occupational Safety and Health (NIOSH) based on:
  - Increasing widespread use as an alternative to glutaraldehyde in the sterilization of heat sensitive medical and dental equipment
  - Limited availability of toxicology data
- Study recommendations:
  - Toxicological characterization including studies to assess dermal irritation, dermal toxicity, sensitization, and asthmagenic potential



Background

- OPA has been suggested as a replacement for glutaraldehyde
  - Glutaraldehyde induces allergic contact dermatitis, skin and respiratory sensitization and irritation, eye irritation, and occupational asthma
- Approved by the U.S. FDA and available for use as a high-level disinfectant since 1999
  - Technical formulation contains 0.56% OPA (w/v)
- Safety of OPA based on unpublished toxicological data provided to the FDA and EPA as confidential business information
- Safety relative to glutaraldehyde not based on comparative toxicology studies
  - Greater potency of OPA compared to glutaraldehyde
  - Use of lower concentrations, contributing to a low vapor pressure

Significance and Public Health Impact

- Use of OPA is widespread and increasing
- Virtually no publicly available data on the safety of OPA
- Reports of health care workers and patients experiencing toxic effects following exposure to OPA
  - FDA approval for medical devices, not workplace exposures
- NTP program complements and integrates with NIOSH's planned efforts
  - Assessment of work practices associated with OPA
  - Exposure characterization and assessment
  - Development of air and surface monitoring methods
  - Immunological assessment of exposed healthcare workers
- Provide a basis for the determination of safe workplace exposure limits for OPA and the development of guidance for occupational and healthcare workers using OPA

Toxicology Studies of OPA – Limited Availability of Data

- Available summaries suggest that formulated product (0.56% OPA) is non-sensitizing and non-irritating to skin; high oral and dermal LD_{50}
- MSDS suggests that OPA (>99% purity) is a skin, eye, respiratory, and mucous membrane irritant
- Other available summaries concluded that OPA (preparation not specified):
  - Not mutagenic
  - No developmental toxicity
  - Poor dermal absorption
- Based on properties of aldehydes including glutaraldehyde, reasonable to assume that OPA may cause:
  - Dermal and respiratory sensitization
  - Exacerbation of asthma or bronchitis

Human Health Effects Associated with OPA Exposure

- Adverse effects in healthcare workers
  - Irritant-associated effects
  - Occupational bronchial asthma and contact dermatitis
- Adverse effects in patients exposed to OPA disinfected instruments
  - Contact irritation and allergic reactions in patients
  - Post-marketing surveillance reported patients experiencing anaphylaxis-like reactions
    - 24 out of 1 million undergoing repeated cystoscopy for urological procedures

Hypothesis

OPA induces dermal and respiratory irritation and sensitization, and similar toxicities as observed for glutaraldehyde

Proposed Program

- Determine vapor pressure of OPA in solution
  - Workplace-relevant concentrations of OPA
- Investigate the potential for OPA to cause dermal and respiratory sensitization in rodent models
  - Consider comparative studies with glutaraldehyde

Proposed Program

- Conduct absorption, distribution, metabolism and elimination (ADME) studies in rodents
  - Determine systemic exposure
- Conduct repeat-dose studies in rodents to assess toxicity and potential systemic effects
  - Inhalation studies compared to previous NTP glutaraldehyde studies
  - Dermal studies